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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/863,777	05/23/2001	James W. Felt	10498-00012	2435

7590 12/15/2003
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EXAMINER

EPFS FORD, JANET L

ART UNIT	PAPER NUMBER
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1635

DATE MAILED: 12/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

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Office Action Summary	Application No. 09/863,777	Applicant(s) FETT ET AL.	
	Examiner Janet L. Epps-Ford, Ph.D.	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 September 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14 and 24-32 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9, 11, 13, 14 and 24-32 is/are rejected.
- 7) ☒ Claim(s) 10 and 12 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments

Claim Rejections - 35 USC § 112

2. Claims 1-9, 11 and 13 remain rejected, and claims 24-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record set forth in the Official Action mailed 3-19-2002.
3. Applicant's arguments filed 9-26-03 have been fully considered but they are not persuasive. Applicants traverse the instant rejection on the grounds that the "[w]ritten description requirement does not require the applicant to describe in the specification exactly the subject matter claimed. Instead, the description must clearly allow persons of ordinary skill in the art to recognize that the inventor invented what is claimed. Well known information need not be repeated in the specification." Moreover, in regards to the human angiogenin sequence reading on polymorphic, splice, or allelic variants of human angiogenin, Applicants argue that no such disclosure is required. Additionally, Applicants argue that "additional oligonucleotides within the scope of this invention can be prepared by first selecting a target sequence anywhere along the known nucleic acid sequence of the angiogenin gene." Contrary to Applicant's assertions, the instant claims recite "[A] compound for inhibiting expression of angiogenin comprising an oligonucleotide or analog thereof having a base sequence complementary to a target portion of a

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nucleic acid encoding human angiogenin.” It therefore, follows that each additionally oligonucleotide prepared by the guidance provided in the specification as filed would also have to be tested to determine whether or not it would function to inhibit the expression of the human angiogenin gene. Simply because an oligonucleotide may have a base sequence that is complementary to a target sequence, does not mean that the oligonucleotide would necessarily have functional activity to inhibit the expression of the target gene, the presence of this functional activity must be determined empirically.

Additionally, Applicants have not demonstrated that the specific compounds disclosed by Applicants in the specification as filed, i.e. that are complementary to the human angiogenin nucleic acid set forth in Figure 1, define a structure that is correlated with the function of inhibiting the expression of all variants of angiogenin nucleic acid.

In the instant case, Applicants are only in possession of antisense oligonucleotides targeting the nucleic acid sequence of human angiogenin as set forth in Figure 1 of the specification as filed. Further experimentation, is required in order for applicants to determine antisense oligonucleotides targeting these polymorphic and allelic variants of angiogenin nucleic acid. Therefore, since further experimentation is necessary to identify the full scope of compounds encompassed by the claims, at the time of filing of the instant application the full scope of the instantly claimed invention was not “ready for patenting,” or there was not an actual reduction to practice of the full scope of the claimed invention.

Claim Rejections - 35 USC § 103

4. Claims 1-9, 11 and 13 remain rejected, and claims 24-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vallee et al., in view of Olson et al., Milligan et al., Burch, Anderson et al., and Artavanis-Tsakonas et al. for the reasons of record set forth in the Official Action mailed 3-19-2002.

Applicant's arguments filed 9-26-03 have been fully considered but they are not persuasive. Applicants traversed the instant rejection on the same grounds as set forth in the response filed 4-14-03. Therefore, the examiner's response to those arguments is presented below.

Contrary to Applicant's assertions, the prior art clearly provides motivation for exploring the role of human angiogenin expression in regulating tumor growth. As stated previously Olson teach that inhibition of angiogenin is an attractive therapeutic target for the treatment of both primary and metastatic cancer because angiogenesis is crucial in growth and metastatic spread of cancer. Furthermore, Olson et al. teach the use of antibodies to inhibit the expression of angiogenin. Milligan et al. provides a teaching that describes the use of antisense inhibitors to target the expression of a gene, wherein the antisense oligonucleotides can be designed in order to make potential specific therapeutic agents for any disease in which the causative gene is known, in the instant case the gene is angiogenin and the disease is primary and metastatic cancer. In the instant case, in the absence of any evidence of unexpected results, it would have been obvious to substitute one potential inhibitor of angiogenin, in the instant case antisense oligonucleotides, for another (i.e. antibodies) in order to understand the role of this gene in the

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angiogenesis of tumors and for designing potential therapeutics for treating cancer by the design of antisense oligonucleotides targeting the expression of this gene.

One of ordinary skill in the art would have been motivated to further elucidate the function of angiogenin by inhibiting angiogenin gene expression because Olson et al., which does not explicitly teach antisense oligonucleotides that target angiogenin, does suggest inhibiting angiogenin in order to assess the role of angiogenin in tumor growth. Thus what was known particularly about angiogenin and tumor growth, as taught by the references of Vallee et al. and Olson et al., combined with the teaching of Milligan et al. for employing the antisense art, and the disclosures of Burch, Artavanis-Tsakonas et al., and Anderson for modifying oligonucleotides in general, render claims 1-9, 11, 13, and claims 24-32 unpatentable under 35 U.S.C. 103(a).

In addition to repeated the arguments set forth in the response filed 4-14-03, Applicants also traversed the instant rejection on the grounds that the cytotoxicity demonstrated by the claimed compounds in terms of data showing an actual decrease in tumor size in an unexpected result favoring non-obviousness. However, contrary to Applicant's assertions, the unexpected results were specific for administration of the antisense oligonucleotide according to JF2S, having the following sequence 5'- GCCCATCACCATCTCTTC - 3'. Applicant's arguments do not take the place of evidence. Absent evidence to the contrary, oligonucleotides produced according to Vallee et al., in view of Olson et al., Milligan et al., Burch, Anderson et al., and Artavanis-Tsakonas et al. would be expected to possess some degree of inhibitory activity of angiogenin expression, and presumably would also block the secondary effects associated with angiogenin expression, including angiogenesis. Applicant's arguments of unexpected results are

not persuasive, since the assertion is not supported by objective evidence that the oligonucleotides produced by the combination of the Vallee et al., in view of Olson et al., Milligan et al., Burch, Anderson et al., and Artavanis-Tsakonas et al. references, would not be expected to have the same properties as Applicant's claimed compounds.

Conclusion

5. Claims 10, 12 and 14 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

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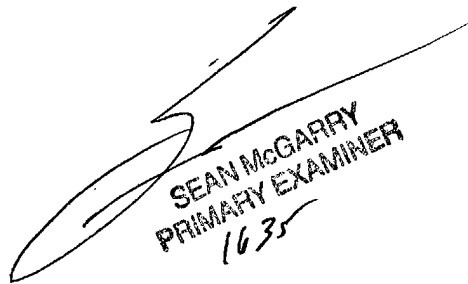
7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford, Ph.D. whose telephone number is 703-308-8883. The examiner can normally be reached on Monday-Thursday, 8:30 AM - 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on 703-308-0447. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Janet L. Epps-Ford, Ph.D.
Examiner
Art Unit 1635

JLE


SEAN MCGARRY
PRIMARY EXAMINER
1635